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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/748,133	12/27/2000	Russell Mumper	50229-207	3309

7590 12/30/2003

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EXAMINER	
BENNETT, RACHEL M	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 12/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/748,133	Applicant(s) MUMPER ET AL.	
	Examiner Rachel M. Bennett	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. In view of the reply brief filed on 6/16/03, PROSECUTION IS HEREBY REOPENED. New grounds of rejections are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Specification

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-1-10, 16-25, 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vora et al. (5,326,737), further in view of Acharya (5,102,666) and Benes et al. (5,639,469).

Applicants claim a pharmaceutical gel composition comprising: a solvent vehicle, at least one water-insoluble swellable mucoadhesive polymer, at least one pH-sensitive film-forming polymer forming a film when applied to skin or a mucosal surface, and at least one molecule of interest.

Vora et al. discloses a method of treating aphthous ulcers and other mucocutaneous disorders. See abstract. Amlexanox can be used to treat aphthous ulcers and other mucocutaneous disorders in the form of a gel. The dosage forms should slowly release the drug to minimize swallowing of the drug and would also lower or eliminate the occurrence of pharmacological or toxicological side effects. See col. 2 lines 64-67. The compositions may contain various ingredients such as diluents, adhesives, viscosity builders, plasticizers, emulsifiers, flavoring agents, and sweetening agents. See cols. 3 and 4. Vora does not teach using a swellable polymer, and a pH-sensitive polymer in the formulation.

Acharya teaches controlled release compositions containing polycarbophil-type (a.k.a. Noveon) component with water in the presence of an active composition. The compositions may be in the form of gels. See col. 1, lines 5-15). The invention also teaches a method of controlled release treatment by use of a polymeric carrier containing an active composition, which is then used to contact an area of skin or mucous membrane to be treated with the active composition. See col., lines 15-25. The compositions of the invention can be provided in the form of a three-dimensional structure such as a film, wherein the active composition is contained in matrix. The

water used in the polycarbophil may be mixed with other co-solvents, such as polyethylene glycol or propylene glycol. See col. 10, lines 61-65.

Benes et al. teaches delivery of a drug, specifically heparin, an anticoagulant across a mucosal surface. It is taught that drugs delivered across oral mucosal avoid hepatic first-pass inactivation, poor or erratic absorption from the gasto-intestinal tract, inactivation by gastro-intestinal fluids, and other modes of inactivation characteristic of oral drug ingestion. See col. 1, lines 15-20. The device of Benes includes means for adhering to mucosal, such as with mucoadhesives. Preferred mucosadhesives include a polymeric resin and hydrophobic elastomeric component. The polymeric resin comprises at least about 55% of carboxylic acid moieties. The carboxylic acid moieties can be present as neutralized carboxylate salts. It is taught that basic polyamines such as Eudragit is suitable in neutralizing a resin. See col. 5, line 11 – col. 6, line 17. Preferred resins include CARBOPOL. See col. 5, lines 66-67.

It is the position of the examiner it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the composition of Vora by adding NOVEON as taught by Acharya or CARBOPOL taught by Benes and a pH –sensitive film forming polymer, EUDRAGIT taught by Benes because of the benefits of delivering drugs across oral mucosal including avoiding hepatic first-pass inactivation, poor or erratic absorption from gastro-intestinal tract, inactivation by gastrointestinal fluids and other modes of inactivation characteristics of oral drug ingestion.

4. Claims 1, 3-11, 14-16, 18-26, 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vora et al. (5,326,737), further in view of Acharya (5,102,666) and Benes et al. (5,639,469) and Mantelle (US 5446070).

Vora et al. discloses a method of treating aphthous ulcers and other mucocutaneous disorders. See abstract. Amlexanox can be used to treat aphthous ulcers and other mucocutaneous disorders in the form of a gel. The dosage forms should slowly release the drug to minimize swallowing of the drug and would also lower or eliminate the occurrence of pharmacological or toxicological side effects. See col. 2 lines 64-67. The compositions may contain various ingredients such as diluents, adhesives, viscosity builders, plasticizers, emulsifiers, flavoring agents, and sweetening agents. See cols. 3 and 4. Vora does not teach using a swellable polymer, and a pH-sensitive polymer in the formulation.

Acharya teaches controlled release compositions containing polycarbophil-type (a.k.a. Noveon) component with water in the presence of an active composition. The compositions may be in the form of gels. See col. 1, lines 5-15). The invention also teaches a method of controlled release treatment by use of a polymeric carrier containing an active composition, which is then used to contact an area of skin or mucous membrane to be treated with the active composition. See col., lines 15-25. The compositions of the invention can be provided in the form of a three-dimensional structure such as a film, wherein the active composition is contained in matrix. The water used in the polycarbophil may be mixed with other co-solvents, such as polyethylene glycol or propylene glycol. See col. 10, lines 61-65.

Benes et al. teaches delivery of a drug, specifically heparin, an anticoagulant across a mucosal surface. It is taught that drugs delivered across oral mucosal avoid hepatic first-pass inactivation, poor or erratic absorption from the gasto-intestinal tract, inactivation by gastro-intestinal fluids, and other modes of inactivation characteristic of oral drug ingestion. See col. 1, lines 15-20. The device of Benes includes means for adhering to mucosal, such as with

mucoadhesives. Preferred mucosadhesives include a polymeric resin and hydrophobic elastomeric component. The polymeric resin comprises at least about 55% of carboxylic acid moieties. The carboxylic acid moieties can be present as neutralized carboxylate salts. It is taught that basic polyamines such as Eudragit is suitable in neutralizing a resin. See col. 5, line 11 – col. 6, line 17. Preferred resins include CARBOPOL. See col. 5, lines 66-67.

Vora, Acharya and Benes do not teach the molecule of interest to be an anesthetic, an antiseptic or a seditive.

Mantelle discloses compositions for topical application comprising therapeutically effective amount of pharmaceutical agents, a pharmaceutically acceptable carrier and a solvent for the pharmaceutical agents. Mantelle discloses the topical application of an anesthetic agent to prevent or ameliorate pain. The composition is administered topically, specifically to the mucosal. Local anesthetic agents include lidocaine, benzocaine and dyclonine. See col. 6, lines 40-51. Solvents are disclosed to be propylene glycol and polyethylene glycol. See cols. 6 & 7. Furthermore, Mantelle teaches any of the following drugs may be used in the pharmaceutical composition: antiseptics, specifically triclosan and sedatives, specifically benzodiazepine.

It is the position of the examiner it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the composition of Vora, Acharya and Benes by adding a anesthetic or antiseptic or sedative agent as taught by Mantelle because of the expectation of preventing or ameliorating pain as taught by Mantelle.

5. Claims 1-10, 12-13, 16-25, 27-29, 31-32 rejected under 35 U.S.C. 103(a) as being unpatentable over Vora et al. (5,326,737), further in view of Acharya (5,102,666) and Benes et al. (5,639,469) and Findlay et al. (5204323).

Vora et al. discloses a method of treating aphthous ulcers and other mucocutaneous disorders. See abstract. Amlexanox can be used to treat aphthous ulcers and other mucocutaneous disorders in the form of a gel. The dosage forms should slowly release the drug to minimize swallowing of the drug and would also lower or eliminate the occurrence of pharmacological or toxicological side effects. See col. 2 lines 64-67. The compositions may contain various ingredients such as diluents, adhesives, viscosity builders, plasticizers, emulsifiers, flavoring agents, and sweetening agents. See cols. 3 and 4. Vora does not teach using a swellable polymer, and a pH-sensitive polymer in the formulation.

Acharya teaches controlled release compositions containing polycarbophil-type (a.k.a. Noveon) component with water in the presence of an active composition. The compositions may be in the form of gels. See col. 1, lines 5-15). The invention also teaches a method of controlled release treatment by use of a polymeric carrier containing an active composition, which is then used to contact an area of skin or mucous membrane to be treated with the active composition. See col., lines 15-25. The compositions of the invention can be provided in the form of a three-dimensional structure such as a film, wherein the active composition is contained in matrix. The water used in the polycarbophil may be mixed with other co-solvents, such as polyethylene glycol or propylene glycol. See col. 10, lines 61-65.

Benes et al. teaches delivery of a drug, specifically heparin, an anticoagulant across a mucosal surface. It is taught that drugs delivered across oral mucosal avoid hepatic first-pass inactivation, poor or erratic absorption from the gasto-intestinal tract, inactivation by gastro-intestinal fluids, and other modes of inactivation characteristic of oral drug ingestion. See col. 1, lines 15-20. The device of Benes includes means for adhering to mucosal, such as with

mucoadhesives. Preferred mucosadhesives include a polymeric resin and hydrophobic elastomeric component. The polymeric resin comprises at least about 55% of carboxylic acid moieties. The carboxylic acid moieties can be present as neutralized carboxylate salts. It is taught that basic polyamines such as Eudragit is suitable in neutralizing a resin. See col. 5, line 11 – col. 6, line 17. Preferred resins include CARBOPOL. See col. 5, lines 66-67.

Vora, Acharya and Benes do not teach the molecule of interest to be hirudin.

Ward discloses direct thrombin inhibitors such as hirudin, bivalirudin, and heparin. Hirudin has several advantages over heparin. Heparin does not inhibit clot-bound thrombin, due to the stoichiometry of the heparin-antithrombin-III complex, and is neutralized by platelet factor-4, which is secreted by activated platelets. In clinical trials, acute complications after routine angioplasty were reduced by 39% when hirudin was used rather than heparin.

It is the position of the examiner it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the composition of Vora, Acharya and Benes by substituting hirudin as taught by Ward for the heparinic anticoagulant because of the expectation of inhibiting clot-bound thrombin as taught by Ward.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel M. Bennett whose telephone number is (703) 308-8779. The examiner can normally be reached on Monday through Friday, 8:00 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

rmb

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